

Application No. 10/596,077
Amendment dated March 8, 2010
Reply to Office Action of October 7, 2009

Docket No.: 06290/0204400-USO

REMARKS

Reconsideration is respectfully requested. Claims 41 and 42 have been canceled, without prejudice or disclaimer. Claim 1 has been amended to incorporate the subject matter of now-canceled claim 41. Claim 1 has also been amended to specify agitation “which maintains solvent and PHA cellular biomass in suspension and in contact.” Support for this amendment can be found in the specification at p. 23, lines 1-7. Claim 1 has also been amended to recite “cooling by expansion, through heat exchange with another cooler stream and/or by cooling by means of heat exchangers.” Support for this amendment can be found in the specification at p. 15, lines 10-14. Claim 1 has also been amended to specify that microfiltration in step (iv) occurs at 45° C or less. Support for this amendment can be found in the specification at, for example, p. 28, lines 16-21. Claim 1 has also been amended to recite that the purity of PHA particles in step (vi) is 99% or higher and that the recovery rate of PHA particles is 90% or greater. Support for this amendment can be found in the specification at, for example, p. 18, lines 2-9. Claims 9, 13, 38, and 43 have been amended to correct typographical errors. Claim 43 has been amended to recite “ppm” rather than “pm”. Claim 44 has been amended for clarity and to recite “poly-3-hydroxybutyrate (PBS)” and explicitly recite the process steps of claim 1. No new matter is introduced by these amendments. Claims 1-40, 43, and 44 are currently pending.

Information Disclosure Statement

In the Office Action, the Examiner notes that the Information Disclosure Statement (IDS) filed on November 14, 2009, assumedly having 9 references, fails to comply with 37 CFR 1.98(a)(1), because it lacks a list of all patents, publications, applications, or other information submitted for consideration by the Office. The Examiner indicates that Form 1449 of the IDS of November 14, 2006 (the Examiner identifies this as IDS of November 14, 2009) was missing and needs to be resubmitted. Applicant notes that the USPTO had mis-scanned the filed SB08 (1449), resulting in only blank pages being scanned. As requested by the Examiner, Applicant hereby submits as an attachment the SB08 form originally filed on November 14, 2006. Applicant further notes that PAIR indicates that the USPTO received copies of the non-patent literature references and foreign references on November 14, 2006.

Amendments to the Specification

The specification has been amended to address an error in the paragraph beginning at page 25, line 9. Specifically, the specification refers to a starting biomass slurry containing PHA with a molecular weight at minimum of about 850,000 Da. This is clearly in error given that the obtained PHA has a molecular weight of 850,000 Da. The specification has been amended to correct this error, and now specifies a biomass slurry containing PHA with a molecular weight at minimum of about 1,000,000 Da. Support for this amendment can be found in the Examples, which clearly state the starting molecular weights of PHBs (a representative type of PHA) in biomass to be about 1,000,000 Da (*see*, for example, specification at p. 26, line 24; p. 32, line 22; p. 34, line 29; p. 42, line 2).

The specification has also been amended to address an error in the paragraph beginning at page 26, line 16. Specifically, the specification refers to PHA containing a molecular weight at minimum of about 750,000 Da. The specification has been amended to correct this error, and now specifies that the molecular weight is at minimum of about 850,000 Da. Support for this amendment can be found in the amendment made to the paragraph beginning at page 25, line 9, as mentioned above.

The specification has also been amended to address a typographical error in the paragraph beginning at page 27, line 15. Specifically, the specification refers to a PHA concentration range of 3.5%-810%. The specification has been amended to correct this error, and now specifies a PHA concentration range of 3.5%-8%.

Applicant submits that no new matter is added by these amendments, and respectfully requests the Examiner to enter these amendments to the specification.

Claim Observation

The Examiner has inquired about the use of “pm” in the claim 43 and whether this indicates “parts per million”. Applicant acknowledges that “pm” indeed refers to “parts per million” and has amended claim 43 accordingly.

Indefiniteness rejection

Claims 1-43 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which is considered the invention. In particular, the Examiner contends that the specification does not sufficiently define certain modifiers as posited in the questions listed below. Applicant respectfully submits that the specification sufficiently defines these modifiers. For the sake of organization and clarity, responses to each question are inserted following each respective question.

(a) As to the final product, what is meant by “purified” (%)?

The Examiner is respectfully directed to the specification (*see* specification at p. 8, lines 2-7), which defines high purity as normally superior to 99%. Furthermore, claim 1 has been amended to recite that the purity of the end product is 99% or greater.

(b) In line 5, what is meant by “vigorous agitation” (time, force exerted)? How is it known this is any more vigorous than other known agitation steps used in producing PHA? Did this step produce amore purified PHA?

“Vigorous agitation” is a very common term in the art, and refers to agitation sufficiently strong to maintain the biomass (containing the PHA) in suspension and in close contact with the solvent. Claim 1 has been amended to recite agitation which maintains solvent and PHA cellular biomass in suspension and in contact, for which support can be found in the specification at p. 23, lines 1-7.

(c) In line 5, what is meant by “quick heating” (time, temperature)? How is it known this is any faster or hotter than other known agitation steps used in producing PHA? Did this step produce a more purified PHA?

Claim 1 has been amended to remove the qualifier “quick” from “quick heating”.

Application No. 10/596,077
Amendment dated March 8, 2010
Reply to Office Action of October 7, 2009

Docket No.: 06290/0204400-US0

(d) In line 6, what is meant by “rupture of walls of the cellular biomass”? Is this not arrived at in other known methods of making PHA, in order to recover the same?

Applicant submits that the meaning of the expression “rupture of wall of the cellular biomass” is clear from the wording of step (v) of claim 1, which provides that the step is adequate to obtain a suspension containing PHA granules of high porosity and which are brittle and easily shearable. That is, the step generates PHA granules whose porosity, brittle characteristics, and rapid and adequate rupture allows a suspension of much finer PHA particles which can be washed abundantly during the evaporation process of the PHA solvent to be obtained (*see* specification at p. 27, lines 29-35; p. 28, lines 1-2).

(e) In line 1, what is meant by “rapidly cooling”? How is it known this is any more rapid or colder than other know agitation steps used in producing PHA? Did this step produce a more purified PHA?

The specification discloses that “rapidly cooling” refers cooling a solution in some seconds, by expansion, through heat exchange with another cooler stream and/or by cooling by means of heat exchangers. Claim 1 has been amended to recite “cooling by expansion, through heat exchange with another cooler stream and/or by cooling by means of heat exchangers,” which is supported by the specification at p. 16, lines 10-14. According to equation 3 (*see* specification at p. 9, line 9), the shorter the exposition time of the dissolved PHA to an elevated temperature is, the higher the molecular weight of the product obtained.

(f) In line 12, what is meant by the “temperature which is sufficient to substantially precipitate all the dissolved PHA”? What IS this temperature/range?

The phrase “temperature which is sufficient to substantially precipitate all the dissolved PHA” in step (iii) refers to a temperature that allows for most, but not necessarily all, of the

Application No. 10/596,077
Amendment dated March 8, 2010
Reply to Office Action of October 7, 2009

Docket No.: 06290/0204400-US0

would be expected to impart distinctive structural characteristics to the final product.

Claim 44 is not anticipated by the cited references because the claimed process of obtaining PHB imparts unexpected properties to the PHBs. As amended, claim 1 calls for a PHB with a purity of 99% or greater and a minimum molecular weight of about 850,000 Da obtained from a biomass containing PHB with a molecular weight at minimum of about 1,000,000 Da. Applicant submits that none of the references or passages cited by the Examiner explicitly or inherently disclose PHBs with these combined properties. Therefore, the claimed PHB is imparted with distinctive structural characteristics imparted by the claimed process steps. Importantly, these properties are imparted to the claimed PHBs due to the specific recited steps, which none of the cited references disclose in entirety, carried out as called for in the claimed process. Furthermore, claim 44 has also been amended to recite that the PHB is obtained at a recovery rate of 90% or greater. Applicant submits that the claimed recovery rate results from the specific steps recited in the claims and that the cited references fail to disclose recovery of PHBs at the claimed recovery rate.

In view of the forgoing, claim 44 is not anticipated by the cited references. Therefore, Applicant respectfully requests that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102/103

Claims 1-43 have been rejected under 35 U.S.C. 102 as anticipated by, or in the alternative, as obvious over Horowitz I, Horowitz II, Horowitz III, Traussnig, and Blauhut. According to the Examiner, it would have been obvious to perform the disclosed steps or optimize conditions thereof to recover the claimed PHA species.

The rejection is traversed and reconsideration is respectfully requested.

As a first matter, the rejection of claims 41 and 42 is moot because these claims have been canceled.

Claims 1-40, 43, and 44 are not anticipated by the 5 cited references because they fail to teach each and every step of the claimed process. For instance, none of the cited references teach, *inter alia*, a microfiltration step at a temperature of 45°C or less during the extraction process. Furthermore, claim 1 has been amended to recite that the step of heating the biomass, rupturing the

Application No. 10/596,077
Amendment dated March 8, 2010
Reply to Office Action of October 7, 2009

Docket No.: 06290/0204400-US0

dissolved PHA to precipitate. That is, an infinitesimal quantity of excess PHA (ppm or ppb) may remain dissolved in the solvent during the precipitation step. The Examiner is directed to the Examples, which sufficiently demonstrate that the temperature sufficient to substantially precipitate all of the dissolved PHA is 45°C or lower (*see*, for example, specification at p. 31, lines 21-25; p. 32, lines 7-10).

(g) In line 16, what is the temperature and force/time of the “heating and agitation” step? How is it known this is any hotter or more vigorous than other known agitation steps used in producing PHA? Did this step produce a more purified PHA?

The temperature at which heating occurs in the “heating and agitation” step referred to by the Examiner depends on a number of variables: the binary mixture composition, which is constituted by a water-based solvent, the local atmospheric pressure, and the effluent vapor of the extraction steps. For instance, if the solvent being used is one of the preferred embodiments of the present invention, 3-methyl-1-butanol (isoamyl alcohol), at the beginning of the process, then the operating temperature is about 94-95°C and the process is completed at the temperature of the water, which at sea level is 100°C. Support can be found in the specification at p. 21, line 26-35 to p. 22, line 3, which defines that heating should be sufficient to provoke the heating of the biomass to a temperature between about 90 °C and the boiling temperature of the solvent, under an agitation that should be vigorous, in order to form the liquid, the solid, and the vapor phases.

(h) In line 19, what is meant by “agitation and shearing, so as to rapidly break them (PHA granules)? How is it known this is any more vigorous than other known agitation steps used in producing PHA? Did this step produce a more purified PHA?

The Examiner is respectfully directed to the specification (*see* specification at p. 27, line 29 to p. 28, line 12), which describes the process of shearing PHA granules to provide a suspension of much finer PHA particles.

Application No. 10/596,077
Amendment dated March 8, 2010
Reply to Office Action of October 7, 2009

Docket No.: 06290/0204400-US0

Given the foregoing, Applicant submits that claims 1-43 are indefinite, and respectfully requests that this rejection be withdrawn.

Claim 9 has been rejected as indefinite for reciting the phrase "90o". In response, claim 9 has been amended to recite "90°C". Applicant respectfully requests that this rejection be withdrawn.

Claim 44 has been rejected as lacking antecedent basis for "PHB". In response, claim 44 has been amended to recite "poly-3-hydroxybutyrate (PHB)". Applicant respectfully requests that this rejection be withdrawn.

Anticipation rejection

Claim 44 has been rejected under 35 U.S.C. 102(b) as anticipated by the following 5 references:

1. U.S. Patent No. 6,323,276 to Horowitz et al. ("Horowitz I")
2. U.S. Patent No. 6,228,934 to Horowitz et al. ("Horowitz II")
3. U.S. Patent No. 6,368,836 to Horowitz et al. ("Horowitz III")
4. U.S. Patent No. 4,968,611 to Traussnig et al. ("Traussnig")
5. U.S. Patent No. 5,213,976 to Blauhut et al. ("Blauhut")

According to the Examiner, these references recover the same PHA species products as presently claimed, specifically PHB and PHBV.

The rejection is respectfully traversed and reconsideration is respectfully requested.

According to MPEP §2113, differences in physical and structural properties are important distinctions when considering the patentability of a product-by-process claim. Specifically, §2113 states:

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps

Application No. 10/596,077
Amendment dated March 8, 2010
Reply to Office Action of October 7, 2009

Docket No.: 06290/0204400-USO

cell walls, and dissolving the PHA is carried out in a time sufficiently short to allow a PHA with a molecular weight at a minimum of about 850,000 Da to be obtained from a biomass containing PHA with a molecular weight at a minimum of about 1,000,000 Da, and that the purity of the end PHA product is 99% or greater with a recovery rate of 90% or greater. Again, none of the cited references disclose a step of processing the biomass such that a PHA with a molecular weight higher than 850,000 Da is obtained from biomass containing a PHA with a molecular weight at a minimum of about 1,000,000 Da, or that PHAs with a purity of 99% or greater would be recovered at a rate of 90% or greater. Thus, none of the cited references anticipate the pending claims.

Not only are claims 1-40, 43, and 44 not anticipated by the cited references, they are not obvious over them either. The claimed process calls for a series of steps that synergize to impart unexpected results and unexpected properties to the end PHA product. That is, the steps of the claimed process, when taken together, allow for pure PHA polymer particles of very high molecular weight to be obtained and allow for a high recovery rate of end products. As set forth above, the pending claims as amended call for conditions that allow PHAs with a minimum molecular weight of about 850,000 to be obtained from biomass containing PHAs with a molecular weight at a minimum of about 1,000,000 Da, PHA particles with a purity of 99% or greater, and a recovery rate of 90% or greater. Importantly, the claimed process would not be arrived at by modifying the cited references since the references fail to teach or motivate one of ordinary skill to perform all recited steps. This is significant because all recited steps are required to achieve PHA particles with the claimed properties and recovery rates.

Among others, an important step in the claimed process is the microfiltration step carried out during the extraction process. As called for in the pending claims, microfiltration occurs after the PHA-containing solvent has been cooled to 45°C or less, a temperature range at which PHAs have precipitated in the solvent. This step is significant because it allows the filtered extract to be recovered immediately after PHA extraction from cells and to be dissolved in the solvent, thus allowing for the retention of high molecular weight PHAs by keeping the time of exposure to hot solvent very short (*see*, for example, specification at p. 25, lines 14-27). Moreover, the microfiltration step allows for the removal of significant amounts of solvent contained in the PHB suspension without adverse effects on the polymer, i.e., conserving characteristics such as molecular

weight, poly-dispersability, and fluidity index. This results in a concentrated paste of precipitated PHA, which can then be subjected to washing, heating, and agitation, having the effect of generating PHA granules that have high porosity, are brittle, and are easily shearable. This step allows highly pure, high molecular weight PHA particles to be obtained at a high recovery rate. Notably, none of the cited references teach this important microfiltration step during the extraction process.

As further illustration of the significance of the microfiltration step during extraction, every 1000 liters of suspension submitted to the microfiltration process results in 750-800 liters of solvent removed, leaving 250-285 liters of the suspension. Thus, the exposure to high temperature in the subsequent step of removing the residual solvent by means of washing with vapor and water (step (v)) is kept minimal, preventing further degradation of PHB molecular weight. This is significant because it allows for a polymer with the claimed qualities to be obtained at the claimed recovery rate.

Furthermore, the cited references do not teach all of the required steps that allow PHAs with the claimed properties to be obtained. Horowitz I and II are directed to a method for producing a suspension of predominantly amorphous particles (e.g., PHAs) by thermal treatment, rather than to the extraction and purification of PHAs. As such, they fail to teach, *inter alia*, the steps of processing the live biomass as recited in step (i), microfiltration, and separating the purified PHA particles from the suspension. Furthermore, they provide no teaching or direction that would motivate one of ordinary skill in the art to include these steps in order to produce PHAs with the claimed properties at the claimed recovery rate.

Horowitz III is directed to recovering PHAs from biomass involving the treatment the PHAs with ozone. In addition to lacking the microfiltration step of the claimed process, Horowitz III fails to teach the unexpectedly pure, high molecular weight PHAs (i.e., minimum of about 850,000 Da) that are recovered at a rate of 90% or greater by the claimed process. Similarly, Blauhut is directed to a process for recovering PHAs from microorganisms and also fails to teach a microfiltration step as recited in the claimed process, and is also silent as to the molecular weights of PHAs that are obtained. *See In re Burt*, 356 F.2d 115, 121 (CCPA 1966) ("Silence in a reference is hardly a proper substitute for an adequate disclosure of facts from which a conclusion of obviousness may

justifiably follow.”). Furthermore, one of ordinary skill in the art would not reasonably expect that Horowitz III’s process would allow for the efficient recovery of highly pure, high molecular weight PHAs as called for in the pending claims. This is especially true given that all Examples disclosed in Horowitz III employ the use of a nuclease (*see* Examples 1 and 5) or pulverization (*see* Example 7) to rupture the cell wall. The steps of agitation and quick heating as called for in the pending claims allow for the quick rupture of cell walls, thus minimizing processing time which reduces damage to the PHA polymers.

Traussnig is directed to the process of extracting PHA from microorganisms. As such, it lacks any teaching of processing the precipitated PHA granules by agitation and shearing, which is essential for the claimed high recovery rate of high molecular weight PHAs. Furthermore, the pending claims as amended call for processing conditions that allow for PHAs at a purity of 99% or greater with a minimum molecular weight of about 850,000 Da to be obtained at a recovery rate of 90% or greater. Traussnig provides no teaching that the disclosed process allows for such high molecular weight PHAs to be obtained. In fact, none of the Examples disclosed in Traussnig allow for obtaining high molecular weight PHAs called for in the pending claims (*see* Examples 1-8). That is, none of the Examples disclose obtaining PHAs with a molecular weight at a minimum of about 850,000 Da, supporting the unexpected synergism conferred by the recited steps of the claimed method.

Furthermore, the claimed process is not obvious over the cited prior art because it satisfies a long-felt need to carry out the efficient recovery of PHAs at an industrial scale. As disclosed in the Examples, when the claimed process is conducted at an industrial scale, recovery rates higher than 95% are achieved (*see*, for example, specification at p. 36, line 33 to p. 38, line 8; p. 40, line 20 to p. 41, line 30). Notably, the cited prior art references fail to show that their respective processes would be successful at an industrial scale, much less achieve recovery rates of 90% or greater.

In view of the foregoing, claim 1 is not anticipated or obvious over the cited references. Claims 2-40, 42, and 43 directly or indirectly depend from claim 1, and are thus not anticipated or obvious over the cited references for the same reasons. Therefore, Applicant respectfully requests that this rejection be withdrawn.

Application No. 10/596,077
Amendment dated March 8, 2010
Reply to Office Action of October 7, 2009

Docket No.: 06290/0204400-US0

CONCLUSION

In view of the above remarks, it is respectfully requested that the application be reconsidered, and that all the pending claims be allowed and the case passed to issue.

If there are any other issues remaining that the Examiner believes can be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: March 8, 2010

Respectfully submitted,

By



Thomas L. Bean

Registration No.: 44,528
DARBY & DARBY P.C.
P.O. Box 770
Church Street Station
New York, New York 10008-0770
(212) 527-7700
(212) 527-7701 (Fax)
Attorneys/Agents For Applicant

ATTACHMENTS